

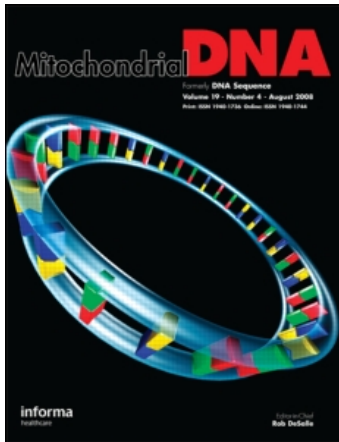
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Mitochondrial DNA

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Mito-communications

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Mito-communications

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“Bottlenecking” mitochondria

In a vast majority of cases, individual organisms contain a single mitochondrial DNA (mtDNA) molecular type (one mtDNA nucleotide sequence per organism). This property, known as homoplasmy, is one of the primary characteristics of mtDNA. A striking observation is that while genetic variants are obviously expected to appear regularly in any individual as a result of the mutation process, homoplasmy is maintained across generations. Besides, descendants of heteroplasmic mothers themselves generally turn back to homoplasmy after a few generations (White et al. 2008). This has led to the idea that, at some point of the female germline development, mtDNA molecules undergo a severe genetic bottleneck whose modalities are somewhat controversial (Khrapko 2008). Wai et al. (2008) have recently provided crucial data that reveal the “when”, if not the “how”, of this phenomenon.

Wai et al. (2008) followed the entire development of heteroplasmic mice germlines from embryonic stage E8.5 (8.5 days after fertilization) to postnatal stage P25 (25 days after birth) and fertilization. Not only did they determine the mtDNA copy number in single germ cells but also the genotypic variance associated with each developmental stage, a task not so far undertaken. They were able to show that the mtDNA count per cell dramatically decreases in primordial germ cells (at least 700-fold with respect to the mtDNA copy number in the fertilized oocyte), then steadily increases (10–20-fold) until the colonization of the gonad (around stage E13.5), and finally rises to 175,000 units per mature oocyte. Meanwhile, the genotypic variance, which was used by the authors to measure the segregation of mtDNA variants (i.e. identify the genetic bottleneck), did not exhibit any

significant change during the physical bottleneck occurring in primordial germ cells. On the contrary, it increased significantly during the first stages of postnatal folliculogenesis, concomitantly with the expansion of the mtDNA population.

The authors thus propose a model in which homoplasmy would mostly arise as a consequence of the random growth of a subpopulation of mtDNAs during folliculogenesis, independently of the embryonic physical bottleneck—which might, however, help in filtering severe deleterious mutations from the mtDNA pool. Interesting developments can be expected that will clarify the way this subpopulation replication is favored.

Reference

- Khrapko K. 2008. Two ways to make an mtDNA bottleneck. *Nat Genet* 40:134–135.
- Wai T, Teoli D, Shoubridge EA. 2008. The mitochondrial genetic bottleneck results from replication of a subpopulation of genomes. *Nat Genet* 40:1484–1488.
- White DJ, Wolff JN, Pierson M, Gemmel NJ. 2008. Revealing the hidden complexities of mtDNA inheritance. *Mol Ecol* 17: 4925–4942.

Diluting paternal mitochondria

In sexually reproducing organisms, maintaining mtDNA uniformity not only necessitates eliminating new mtDNA variants arising in germlines but also that only one of the sexes (generally females) contributes to the mtDNA pool of the next generation. Because both sperms and oocytes contain mitochondria, animals have evolved mechanisms that aim at impeding male transmission of mtDNA. Failure of these mechanisms

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(referred to as paternal leakage) can be compensated for by the elevated dilution of paternal mtDNA in the zygote, since mature oocytes contain enormous quantities of maternal mtDNA (see above). Despite the importance of the ratio of paternal-to-maternal mtDNA for our understanding of mtDNA inheritance, this relationship had only been estimated in mice and humans. Wolff and Gemmel (2008) have recently determined this ratio in chinook salmon.

To do so, they used quantitative PCR to assess the number of mtDNAs per oocyte. Targeting a short *nd1* fragment in a total of 85 oocytes sampled from 17 individuals, they showed that their average content in mtDNA was $3.2 \pm 1.0 \times 10^9$ molecules per cell. The authors report that this figure exceeds by at least three orders of magnitude that reported in mammals, which makes sense if one considers reproductive strategies (external versus internal fertilization and growth) and simple metric aspects (oocyte diameter comprised between 4.5 and 5.5 mm versus between 0.07 and 0.12 mm). In a previous analysis of sperm mtDNA content, the same authors had shown that male germ cells contain 5.73 ± 2.28 molecules per cell (Wolff and Gemmel 2008), which is close to the estimated mtDNA content of mammalian sperm cells. Accordingly, ratios of paternal-to-maternal mtDNA in the fertilized egg also differ by at least three orders of magnitude between mammals and chinook salmon, making paternal leakage in salmon more unlikely than in mammals.

The authors rightly emphasize that a better knowledge of the extent of this dilution effect among animal taxa would allow a better taxon-specific assessment of the risk of paternal leakage.

Reference

- Wolff JN, Gemmel NJ. 2008. Estimating mitochondrial DNA content of chinook salmon spermatozoa using quantitative real-time polymerase chain reaction. *Biol Reprod* 79:247–252.
- Wolff JN, Gemmel NJ. 2008. Lost in the zygote: The dilution of paternal mtDNA upon fertilization. *Heredity* 101:429–434.

Making another exception to mitochondrial homoplasmy

If homoplasmy is undoubtedly the rule, transient heteroplasmy cannot qualify as rare. On the other hand, stable heteroplasmy is certainly scarce among animals. A well-characterized case so far is that of bivalves, manifested by doubly uniparental inheritance

of mtDNA (reviewed by Breton et al. 2007). Another exceptional case of inherited heteroplasmy has been unveiled by an article recently published in *PLoS ONE* (Doublet et al. 2008).

Doublet et al. (2008) were first surprised to observe that a polymorphism (11973G/A) occurring in a tRNA anticodon seemed to be shared by *Armadillidium vulgare* (Isopoda, Crustacea) individuals of varying geographic origin. Extending their study to other isopod crustacean species whose last common ancestor is believed to have lived at least 30 million years ago, they showed by DNA sequencing and PCR-restriction fragment length polymorphism that the 11973G/A heteroplasmy was a common feature of the group. In addition to that, the inheritability of this character was monitored at the laboratory over three generations of *A. vulgare*. It was also well established that the observed heteroplasmy resulted from the presence of two actual mitochondrial variants (i.e. not from the co-amplification of a mitochondrial pseudogene). Finally, contrarily to what is observed in bivalves, male and female *A. vulgare* gonadal tissues were found to be heteroplasmic, ruling out the possibility of doubly uniparental inheritance of mtDNA.

The authors thus describe a truly new form of stable heteroplasmy, which they link to the trimeric structure of this crustacean mitogenome (three 14-kb monomers, of which two are fused in opposite polarities). Interestingly, they note that the two variants (11973G and 11973A) identified in their study encode two tRNAs (tRNA-Ala and tRNA-Val) that would otherwise be absent from the mitochondrial genome. As the lack of any of those two tRNAs is likely to be detrimental to mitochondrial translation, Doublet et al. (2008) suggest the 11973G/A heteroplasmy might have been maintained for more than 30 million years through balancing selection. Although exceptional, this case argues in favor of a more detailed depiction of the origin of observed heteroplasmy.

For a recent review on mtDNA inheritance, its general rules and exceptions, please see White et al. (2008).

Reference

- Breton S, Doucet Beaupré H, Stewart DT, Hoeh WR, Blier PU. 2007. The unusual system of doubly uniparental inheritance of mtDNA: Isn't one enough? *Trends Genet* 23:465–474.
- Doublet V, Souty-Grosset C, Bouchon D, Cordaux R, Marcadé I. 2008. A thirty million year-old inherited heteroplasmy. *PLoS ONE* 3:e2938.
- White DJ, Wolff JN, Pierson M, Gemmel NJ. 2008. Revealing the hidden complexities of mtDNA inheritance. *Mol Ecol* 17:4925–4942.